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ARAŞTIRMA YAZISI / RESEARCH ARTICLE

HİPERKALEMİ NEDENİYLE HASTANEYE YATIRILAN KRONİK BÖBREK HASTALIĞI OLAN HASTALARDA HASTANE - İÇİ MORTALİTEYİ ETKİLEYEN FAKTÖRLER

FACTORS AFFECTING HOSPITAL MORTALITY IN PATIENTS WITH CHRONIC KIDNEY DISEASE HOSPITALIZED FOR HYPERKALEMIA

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ÖZET

AMAÇ: Hiperkalemi düzeltilmediği takdirde ölümcül sonuçlara yol açabilen bir elektrolit inbalansıdır. Kronik böbrek hastalığı olan hastalar hiperkalemik olma eğilimindedir. Hiperkalemi nedeniyle hastaneye yatırılan hastalarda hastane-içi mortalite ile ilişkili faktörleri bilmek hiperkaleminin sebep olduğu mortalitede azalma sağlayabilir. Bu çalışmada hiperkalemi nedeniyle hastaneye yatırılan kronik böbrek hastalığı olan hastalarda hastane-içi mortalite ile ilişkili faktörleri araştırmayı amaçladık.

GEREÇ VE YÖNTEM: Ocak 2019 - Nisan 2022 tarihleri arasında nefroloji kliniğine yatırılan ve serum potasyum düzeyi >5.1 mEq/L olan hastalar çalışmaya dahil edildi. Hastalar hastane-içi ölüm gelişen ve yaşayanlar olarak iki gruba ayrıldı. Gruplar laboratuvar, klinik ve demografik özellikler açısından karşılaştırıldı.

BULGULAR: Mevcut çalışma kronik böbrek hastalığı tanısı olan 123 hastayı içermektedir. Katılımcıların yaş ortalaması 65.92±13.7 yıldı. Yaş, diyabetes mellitus, koroner arter hastalığı, hemodiyaliz, potasyum seviyesi, kalsiyum ve pH mortalite açısından bağımsız birer risk faktörü olarak bulundu (sırasıyla p=0.004, p<0.001, p=0.004, p=0.009, p=0.001, p=0.007 ve p=0.008).

SONUÇ: Hiperkalemi nedeniyle hastaneye yatırılan hastalarda mortaliteyi etkileyen faktörlerin iyi bilinmesi ile kötü sonuçlar azaltılabilir. Hastane-içi mortalite riski artmış hiperkalemik hastalarda alınabilecek ek önlemler ve hızlı müdahale ile mortalite riski en aza indirilebilir.

ANAHTAR KELİMELER: Diyabetes mellitus, Hiperkalemi, Mortalite, Yaş

ABSTRACT

OBJECTIVE: Hyperkalemia is an electrolyte imbalance that can lead to fatal results if not corrected. Patients with chronic kidney disease are prone to be hyperkalemic. Knowing the factors associated with hospital mortality in patients hospitalized for hyperkalemia may reduce mortality caused by hyperkalemia. In the present study, we aimed to research the factors associated with hospital mortality in patients with chronic kidney disease hospitalized for hyperkalemia.

MATERIAL AND METHODS: Patients who were hospitalized in the nephrology clinic between January 2019 and April 2022 and whose serum potassium level was >5.1 mEq/L were included in the study. Patients were divided into two groups as in-hospital deaths and survivors. The groups were compared in terms of laboratory, clinical, and demographic characteristics.

RESULTS: The current study includes 123 cases with a diagnosis of chronic kidney disease. The mean age of the participants was 65.92±13.7 years. Age, diabetes mellitus, coronary artery disease, hemodialysis, potassium level, calcium and pH were found to be independent risk factors for mortality (p= 0.004, p< 0.001, p= 0.004, p=0.009, p=0.001, p=0.007,and p=0.008 respectively).

CONCLUSIONS: Poor outcomes can be reduced by knowing the factors affecting mortality in patients hospitalized for hyperkalemia. In hyperkalemic patients with increased in-hospital mortality risk, the mortality risk can be minimized with additional precautions and rapid intervention.

KEYWORDS: Diabetes mellitus, Hyperkalemia, Mortality, Age

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INTRODUCTION

The kidneys are the main organs for keeping the serum potassium level within the normal range. Individuals with chronic kidney disease (CKD) are at higher risk of hyperkalemia than individuals with a normal glomerular filtration rate. (GFR) (1 - 3). In a recent review, it is reported that hyperkalemia is as high as 40 to 50% of patients with CKD (4). The most serious manifestations of hyperkalemia are paralysis and arrhythmias (5, 6).

Cardiac adverse effects of hyperkalemia may range from mild electrocardiographic changes to cardiac arrest. Cardiac manifestations are the main determinants of morbidity and mortality in hyperkalemia (7). Mortality rates may reach up to 67% if hyperkalemia is not treated immediately (8). Hyperkalemia is an independent risk factor for death in hospitalized patients, and mortality rates increase as potassium levels increase (9). In a recent study from China, Zhang et al. revealed that the 1-year risk of all-cause mortality increased 5.39 times in patients with hyperkalemia (10). There is not enough study investigating the risk factors for mortality in CKD patients hospitalized for hyperkalemia in our country.

In our study, we aimed to investigate parameters that may be risk factors for in-hospital mortality in patients with CKD hospitalized for hyperkalemia.

MATERIAL AND METHODS

Patients

Electronic files of all patients admitted to the nephrology clinic between January 2019 and April 2022 were retrospectively analyzed. Cases with a potassium level ≥5.1 mEq/L were included in the study. The potassium level at the time of hospitalization was evaluated. Patients aged <18 years were excluded from the study. Demographical parameters, comorbidities, drug history, and laboratory parameters were recorded. All laboratory tests were analyzed with an automatically integrated analyzer (Cobas 6000, Roche, Switzerland). The files of 682 patients hospitalized in the nephrology clinic between the specified dates were reviewed. One hundred and twenty-three of these patients had potassium levels above 5.1 mEq/L. Patients were divided into two groups; the alive group for patients discharged and the death group for patients who died for any reason in-hospital. CKD was defined as a GFR of less than 60 ml/min/1.73m^2 for at least 3 months. In order to determine the baseline CKD stage, patients who were examined by the nephrology outpatient clinic at least 3 times in the last 1 year were taken into consideration.

Management of Hyperkalemia

All patients were given a diet low in potassium since their hospitalization. Drugs that could increase serum potassium, such as angiotensin-converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB), and non-steroidal anti-inflammatory drugs (NSAID) were discontinued. Patients with oral intake were given 880 mg of calcium polystyrene sulfonate with meals. Calcium gluconate therapy was given to all patients with serum potassium >5 mEq/L. All patients presenting paralysis or cardiac manifestations were treated with emergency hemodialysis for hyperkalemia. In addition, patients with potassium >5.1 mEq/L and peaked T-waves on ECG evaluation were also treated with hemodialysis. Intravenous insulin and dextrose, inhaled beta-2 agonists, and bicarbonate were used to increase the shift of potassium

Ethical Committee

Ethics Committee approval was received at the Local Ethics Committee,(Afyonkarahisar Health Sciences University Clinical Research Ethics Committee, dated 01.07.2022, code of ethics committee: 2011-KAEK-2, meeting number: 2022/8, decision number: 360).

Statistical Analysis

Categorical variables were presented as percentages and frequencies. Continuous variables were checked for normal distribution with the Shapiro Wilk test. Normally distributed continuous variables were presented as mean and standard deviation, and non-normally distributed continuous variables were presented as the median and interquartile range (IQR). Categorical variables were compared with the Chi-squ-

are test. Student t-test was used when comparing normally-distributed continuous variables, and the Mann-Whitney U test was used when comparing non-normally distributed continuous variables. Univariate and multivariate logistic regression analyses were used to investigate the parameters affecting in-hospital mortality. Parameters found to affect in-hospital mortality in univariate analyzes were included in the multivariate analysis. All the p values presented were bidirectional and the values with p<0.05 were expressed as significant. Statistical analyzes were made with SPSS 26.0 package program.

RESULTS

Of the 123 patients, 51.2% (n= 63) were women and 48.8% (n= 60) were men. The mean age of the patients was 65.92±13.7 years. While in-hospital death was seen in 13.8% (n= 17) of the patients, 86.2% (n= 106) were discharged. The group of patients who died were older and had a higher rate of congestive heart failure (CHF), coronary artery disease (CAD), diabetes mellitus (DM), stage 5 CKD and hemodialysis (p= 0.001, p< 0.001, p= 0.003, p< 0.001, p< 0.001 and p<0.001, respectively)**(Table 1)**.

Table 1: Comparison of characteristic features, comorbidities and drug history of groups

Parameters	All (n= 123)	Alive (n= 106)	Death (n= 17)	p
Age, mean±SS	65.92±13.7	64.25±13.6	76.29±9.7	**0.001**
Female gender, %-n	51.2-63	49.1-52	64.7-11	0.299
BMI, kg/m²	28.38±3.1	28.28±2.7	28.88±4.1	0.764
Diabetes mellitus, %-n	56.1-69	50-53	94.1-16	**<0.001**
Hypertension, %-n	84.6-104	83-88	94.1-16	0.468
Coronary artery disease, %-n	30.9-38	25.5-27	64.7-11	**0.003**
Congestive heart failure, %-n	13-16	7.5-8	47.1-8	**<0.001**
Cerebrovasculary disease, %-n	12.2-15	13.2-14	5.9-1	0.691
Baseline CKD stage, %-n				
Stage 3 (GFR= 59-30 ml/min/1.73m²)	17.9-22	20.8-22	0	
Stage 4 (GFR= 29-15 ml/min/1.73m²)	61.8-76	66-70	35.3-6	**<0.001**
Stage 5 (GFR< 15 ml/min/1.73m²)	20.3-25	13.2-14	64.7-11	
CKD etiology, %-n				
Diabetes mellitus	39.8-49	36.8-39	58.8-10	
Hypertension	37.4-46	38.7-41	29.4-5	
Chronic glomerulonephritis	13-16	13.2-14	11.8-2	0.397
Polycyctic kidney disease	6.5-8	7.5-8	0	
Obstructive	3.3-4	3.8-4	0	
Hemodialysis, %-n	41.5-51	33-35	94.1-16	**<0.001**
RAAS inhibitors, %-n	48.8-60	50.9-54	35.3-6	0.299
Beta-Blockers, %-n	61.8-76	59.4-63	76.5-13	0.282
Calcium channel blockers, %-n	46.3-57	47.1-50	41.2-7	0.645
Diuretics, %-n	4.9-6	5.7-6	0	0.539

BMI= body mass index, CKD= chronic kidney disease, RAAS= renin-angiotensin-aldosterone system

The group of patients who died had higher serum potassium and phosphorus levels and they had lower serum calcium, pH, and HCO3 levels (p< 0.001, p<0.001, p= 0.002, p<0.001, and p= 0.039, respectively) **(Table 2)**.

Univariate analysis revealed that age, DM, CAD, CHF, hemodialysis, serum potassium, calcium, and pH were risk factors for mortality (p=0.001, p= 0.008, p=0.002, p=0.006, p=0.001, p<0.001, p=0.001 and p=0.001, respectively). Multivariate analysis showed that age, DM, CAD, hemodialysis, potassium, calcium, and pH were independent risk factors for mortality (p= 0.004, p<0.001, p=0.004, p= 0.009, p= 0.001, p=0.007 and p=0.008, respectively) **(Table 3)**.

Table 2: Comparisons of laboratory parameters of the groups

Parameters	All (n= 123)	Alive (n= 106)	Death (n= 17)	p
Urea (mg/dl)	160.11±54.3	160.03±56.6	160.51±33.3	0.977
Creatinin (mg/dl)	5.07±2.43	5.10±2.6	4.92±1.6	0.939
eGFR (ml/min/1.73 m²)	13.84±10.1	14.34±10.7	10.74±5.2	0.494
Sodium (mEq/L)	134.22±7.3	133.92±7.7	136.12±3.4	0.201
Potassium (mEq/L)	5.86±0.7	5.68±0.5	6.96±0.7	**<0.001**
Alanin aminotransferase (U/L)	14.22±8.2	14.73±8.3	13.06±6.9	0.789
Albumin (gr/dL)	3.60±0.6	3.65±0.6	3.29±0.8	0.059
Calcium (mg/dL)	8.79±1.0	8.87±1.1	8.67±1.0	**0.002**
Phosphorus (mg/dL)	5.14±.1.2	4.96±1.2	6.25±1.2	**<0.001**
PTH (pg/mL)	238.3±250.1	303.5±411.5	227.9±214.5	0.733
Leukocyte (x10³/µL)	8.62±2.4	8.54±2.4	9.17±2.6	0.218
Hemoglobin (gr/dL)	10.38±2.4	10.53±2.4	9.44±2.4	0.088
Platelet (x10³/µL)	238.1±79.8	241.6±84.3	216.3±36.9	0.545
pH	7.29±0.1	7.31±0.09	7.20±0.09	**<0.001**
HCO3 (mmol/L)	16.67±4.4	17.98±4.1	14.02±5.1	**0.039**

eGFR= estimated glomerular filtration rate, PTH= parathormone

Table 3: Univariate and multivariate regression analysis for determining risk factors of mortality

	Univariate		Multivariare	
Parameters	OR (95% CI)	p	OR (95% CI)	p
Age	1.112(1.042-1.186)	**0.001**	1.245(1.012-1.348)	**0.004**
Diabetes mellitus	8.765(2.048-12.015)	**0.008**	5.673(3.567-9.913)	**<0.001**
CAD	5.364(1.810-5.898)	**0.002**	3.142(2.456-5.814)	**0.004**
CHF	1.889(1.298-3.947)	**0.006**	1.679(0.986-4.716)	0.127
Baseline CKD				
Stage 3 (reference)				
Stage 4	1.263(0.765-4.543)	0.998		
Stage 5	1.467(0.907-2.903)	0.657		
Hemodialysis	3.457(2.135-6.770)	**0.001**	3.112(2.145-6.659)	**0.009**
Potassium	9.777(5.813-16.876)	**<0.001**	8.788(6.143-10.978)	**0.001**
Calcium	0.734(0.658-0.811)	0.001	0.872(0.671-0.899)	**0.007**
Phosphorus	2.145(0.918-3.246)	0.787		
pH	7.839(1.317-46.636)	0.001	4.125(2.156-5.713)	**0.008**

CAD= coronary artery disease, CHF= congestive heart failure, CKD= chronic kidney disease

DISCUSSION

In our study, parameters affecting mortality in CKD patients hospitalized in our service due to hyperkalemia were investigated. Although hyperkalemia is an electrolyte imbalance that can increase the risk of mortality on its own, our study was designed considering that some parameters may cause to patient death. A well-known risk factor for mortality in individuals with CKD is potassium itself. A study showed that the 6-month mortality rate in CKD patients with hyperkalemia was 4.3 times higher than in CKD patients without hyperkalemia. They also showed that hyperkalemia increases the risk of death 4.85 times (11). In another study; Einhorn et al showed that the risk of hyperkalemia increased in patients with CKD, and the risk of death increased 1 day after hyperkalemia was detected (12). In our study, we showed that hyperkalemia is an independent risk factor for hospital mortality in CKD hospitalized for hyperkalemia.

In most clinical situations, advanced age is among the risk factors for mortality (13 - 15). It is also among the independent risk factors for mortality in CKD (16). We think that

the frequency of diagnosed or undiagnosed CAD may be high in elderly patients and this may have contributed to in-hospital mortality. In our study, age is among the independent risk factors for in-hospital mortality.

DM is accepted as the equivalent of CAD. DM is still the most important cause of CKD globally. There are numerous meta-analyses showing that DM is an independent risk factor for in-hospital mortality in various diseases (17 - 20). DM is also a risk factor for mortality in CKD (21). This study shows that DM is among the independent risk factors for in-hospital mortality in individuals with CKD hospitalized with hyperkalemia. It can be thought that macrovascular complications of diabetes and microvascular complications such as diabetic nephropathy and diabetic neuropathy may also contribute to mortality in individuals with diabetes.

A significant proportion of deaths in the world are due to cardiovascular events. CAD is one of the cardiovascular disease and it may increase in-hospital mortality (22, 23). Cardiovascular diseases are also the major cause of death in patients with CKD (24, 25). This study revealed that CAD is among the independent risk factors for hospital mortality in CKD with hyperkalemia. For this reason, we think that the cardiac effects of hyperkalemia may occur more easily in CAD patients.

Hemodialysis is a powerful treatment choice in patients with hyperkalemia. It is especially used in patients with serious symptoms such as paralysis and cardiac findings due to hyperkalemia. Hemodialysis itself also has some adverse cardiac side effects (26). Li et al showed that fluctuation of serum potassium may cause cardiovascular mortality in patients treated with peritoneal dialysis (27). The present study showed that hemodialysis is among the independent risk factors for in-hospital mortality in CKD with hyperkalemia. This may be because patients who already have more severe hyperkalemia on dialysis or because of potassium levels drop rapidly after dialysis.

Calcium is cardioprotective from the negative effects of hyperkalemia. This is why the initial treatment of hyperkalemia begins with calcium gluconate. Hypocalcemia increases the cardiac toxicity of hypokalemia (28). We could not find any study in the literature showing whether serum calcium levels would be protective in patients with hyperkalemia. Our study suggests that patients having higher serum calcium levels are more likely to survive.

Metabolic acidosis is one of the complications of CKD and also it is closely associated with mortality in patients with CKD (29). Metabolic acidosis may also exacerbate hyperkalemia by causing potassium outflow from the cell to the outside of the cell. Tangri et al showed that metabolic acidosis is an independent risk factor for CKD progression, renal replacement therapy, and all-cause mortality in stage 3-5 CKD patients with non-dialysis dependence (30). Our study suggests that metabolic acidosis is among the independent risk factors for in-hospital mortality in CKD with hyperkalemia.

Another important finding of our study is the usage rates of renin-angiotensin-aldosterone system (RAAS) inhibitors, such as ACEI and ARB, were similar in death and surviving groups. These drugs are known as reno-cardioprotective, but the most feared side effect is hyperkalemia, which can be seen more frequently, especially in patients with CKD. Our study suggests that the use of RAAS inhibitors does not affect in-hospital mortality in CKD patients hospitalized for hyperkalemia.

The limitations of the current study are as follows. Firstly; it is a single-center study. Secondly; it included a small number of patients and thirdly; it does not include the potassium course of the patients. However, we think that our findings contribute to the literature in terms of hyperkalemia management. In conclusion, our study shows that there are some additional risk factors for mortality in hyperkalemic CKD patients. Higher potassium, higher age, presence of DM, presence of CAD, being treated with hemodialysis, lower calcium and lower pH appear to be independent risk factors for mortality in hyperkalemic CKD patients.

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